REACTIONS WITH AZIRIDINES - 39¹.
RING OPENING OF ACTIVATED 2,2-DIMETHYL AZIRIDINES
BY GRIGNARD REAGENTS. A MECHANISTIC STUDY,

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Abstract - Reaction of activated 2,2-dimethylaziridines 1 with
Grignard reagents RMgHal in boiling THF can yield the products
2 of normal aziridine ring opening, the rearranged opening
products 3, and the methallylamides 4 (isomers of 1). The pro-
duct distribution depends on R, Hal, and experimental condi-
tions, and very strongly on the nature of the activating group
A. It is shown that 1 is opened (reversibly for A = sulfonyl)
forming 10 through a Lewis acid assisted attack of Hal on the
tert carbon of 1 (abnormal opening by Hal). Evidence is pre-
sented to show that 4 as well as 3 come from this intermediate.

INTRODUCTION

In a recent report on the reaction of 1e with Grignard reagents RMgHal Zjawiony et
al.² found the expected "normal" nucleophilic ring opening (2e) with R = benzyl or
alkyl. However, with R = aryl they obtained also the rearranged substitution prod-
ucts 3e. They interpreted the formation of 3e by an attack of the Grignard reagent
on a Schiff base intermediate 5e that was supposed to form thermally at 120-130°C.
This assumption of a thermal formation of 5e is not well compatible both with the
known³ one-step isomerization 1 → 4 for A = acyl or sulfonyl and with the state-
ment of the authors that 4e forms up to at least 50% at higher temperatures.

Recently, we needed a sample of 2aP for a mechanistic study of Friedel-Crafts
reactions. When we caused 1a to react with PhMgBr in THF, we obtained (Scheme 1;
Table 1, run 1) a mixture of 2aP and 3aP along with some 4a. This finding prompted
an investigation⁵ whose results have mechanistic as well as preparative bearings.
The rearranging substitution seems to be an analogue of the known⁶-¹⁰ oxirane re-
arrangements. However, the aziridine case introduces further variables, viz. nu-
cleofugality and basicity of the leaving group NA⁶ as well as structure and steric
demands of the activating group A. So, the present work may shed more light not
only on the aziridine chemistry but also on the oxirane chemistry.

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Table 1. Reactions of Aziridines 1 with an Excess\textsuperscript{a} of RMgHal in Boiling THF.

<table>
<thead>
<tr>
<th>Run</th>
<th>A</th>
<th>R</th>
<th>Hal</th>
<th>Time</th>
<th>Yields\textsuperscript{b} [%]</th>
<th>Yield Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>[h]</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1\textsuperscript{c}</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>Br</td>
<td>4</td>
<td>(48)</td>
</tr>
<tr>
<td>2\textsuperscript{d}</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>Br</td>
<td>5.5</td>
<td>(15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22</td>
<td>(28)</td>
</tr>
<tr>
<td>3\textsuperscript{e}</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>Br</td>
<td>4</td>
<td>(58)</td>
</tr>
<tr>
<td>4</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>Br</td>
<td>4</td>
<td>(61)</td>
</tr>
<tr>
<td>5</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>Br</td>
<td>4</td>
<td>(57)</td>
</tr>
<tr>
<td>6</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>Br</td>
<td>5</td>
<td>(63)</td>
</tr>
<tr>
<td>7</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>I</td>
<td>5</td>
<td>(11)</td>
</tr>
<tr>
<td>8</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>I</td>
<td>22</td>
<td>(16)</td>
</tr>
<tr>
<td>9</td>
<td>1a</td>
<td>Ts</td>
<td>Ph</td>
<td>I</td>
<td>96</td>
<td>(8)</td>
</tr>
<tr>
<td>10\textsuperscript{f}</td>
<td>1a</td>
<td>Ts</td>
<td>PhC\textsubscript{2}</td>
<td>HBr</td>
<td>22</td>
<td>36</td>
</tr>
<tr>
<td>11</td>
<td>1a</td>
<td>Ts</td>
<td>Me</td>
<td>I</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>1b</td>
<td>Dcs\textsuperscript{g}</td>
<td>Ph</td>
<td>Br</td>
<td>1</td>
<td>(28)</td>
</tr>
<tr>
<td>13</td>
<td>1b</td>
<td>Dcs\textsuperscript{g}</td>
<td>Ph</td>
<td>Br</td>
<td>22</td>
<td>97</td>
</tr>
<tr>
<td>14</td>
<td>1c</td>
<td>Piv</td>
<td>Ph</td>
<td>Br</td>
<td>4</td>
<td>-</td>
</tr>
</tbody>
</table>

\textsuperscript{a} 5 mmol 1 and 25 mmol RMgHal (prepared from 25 mmol Mg and 25 mmol RHal) in 80 ml THF if not otherwise stated.
\textsuperscript{b} Yields in parentheses from \textsuperscript{1}H-NMR spectroscopic data.
\textsuperscript{c} 10 mmol 1a and 12.5 mmol PhMgBr in 60 ml THF.
\textsuperscript{d} 10 mmol 1a and 10 mmol PhMgBr in 200 ml THF.
\textsuperscript{e} 2.2 mmol 1a and 12.7 mmol PhMgBr in 80 ml THF. Quenching with D\textsubscript{2}O.
\textsuperscript{f} 5 mmol 1a and 17.8 mmol PhCH\textsubscript{2}MgBr in 80 ml THF. The Grignard reagent was prepared from 79 mmol PhCH\textsubscript{2}Br and gave 5.6 mmol bibenzyl.
\textsuperscript{g} Dcs = 2,5-Dichlorobenzenesulfonyl; Piv = COCMe\textsubscript{3}.
RESULTS AND DISCUSSION.

Table 1 shows our results that were obtained in most runs from a large excess of RMgHal. Because of the difficult product separation we estimated the yields of 2aP, 3aP, and 4a in runs 1-9 by ¹H-NMR analysis which allowed a clear distinction of the three products. The most striking features of Table 1 are (1) the influence of the activating group A on the competing substitution reactions as shown by the ratio 2/3 in the second last column of Table 1, (2) the formation of 4 in many runs, and (3) the general absence of products arising from a formal attack of R⁻ on the tert carbon of 1 ("abnormal" opening of 1). The latter point indicates that an SET process¹¹ is not involved.

The yields of 2aP in runs 1-5 show a tendency that suggest a rate dependence on the concentrations of both 1a and PhMgBr, in accord with the bimolecular kinetics of an SN₂ reaction. Such SN₂-like normal opening of 1 is an attack in a distorted neopentyl position. A good leaving group NA⁻ is therefore required to overcome the steric hindrance¹¹,¹². In other words, this SN₂ opening is kinetically favoured by strong activation: Dcs > Ts >> Piv. With A = Dcs (Diclosyl), practically only the normal product 2 is obtained (runs 12 and 13), while with A = Piv no 2 was formed (run 14). It is not clear whether this dramatic product dependence on A is simply a kinetic effect in the formation of 2. A possible retardation of the competing formation of 3 for A = Dcs is considered below in the discussion of Scheme 3. Such a retardation may perhaps be involved also in the marked change of the product ratio 2/3 when going from A = Ts (run 6) to the slightly stronger activating A = Dcs (run 13).

\[ \text{Ligand of Magnesium:} \quad L = \text{Hal or R} \]

The higher yields of 4a in runs 1-3 as compared to runs 4-6 may be correlated with the absence of a large excess of PhMgBr in runs 1 and 2 and with the low concentrations in run 3. i.e. with a slowing down of the reaction that therefore perhaps could not go to completion in runs 1-3. This finding may suggest a transformation of 4 or its anion, respectively, into another product, e.g. into 5 via 7. However, such an explanation is not supported by the results of runs 7-9. An intermediate role of 4a or its magnesium salt could definitely be ruled out when a sample of 4a was recovered unchanged after treatment with a five-fold excess of
PhMgBr or MgBr$_2$ in boiling THF for two days. On the other hand, we cannot exclude such a transformation of 4c under the reaction conditions of Table 1, since the corresponding process has previously been observed for 4d in strongly basic medium$^{14}$. The reason for the probably general difference in isomerization behaviour between N-allylated carboxamides and sulfonamides is supposed to be the large basicity difference of their N-anions. The tautomerization of the N-anion of 4 into the carbanion 4-c$^9$ will be thermodynamically more unfavourable for A = sulfonyl than for A = acyl$^{15}$.

In similar experiments we excluded a simple thermal formation of 4 under the experimental conditions of Table 1. 1a was recovered unchanged after 20 days in boiling THF or 6 days in boiling toluene. A better immediate precursor of 4 would be 8 or its magnesium salt 10, respectively. A solution of 9a in THF gave rapidly a quantitative yield of 4a on addition of aqueous sodium hydroxide solution, thus mimicking the basic conditions of work-up for the reactions of Table 1. This fast dehydrohalogenation is probably the result of an intramolecular E2 mechanism in which the rapidly formed sulfonamide anion of 9a ($pK_a$ of 9a near 11) serves as base. This assumption found support from the same experiment with 9c ($pK_a$ probably about 2.16) that led to only 25% 4c along with 29% unreacted 9c and 31% of what is supposed to be 12 on grounds of $^1$H-NMR data.

If the magnesium salt 10 is the precursor of 4 in the reactions of Table 1, it may also be the precursor of the supposed intermediate 5. Some experiments, whose results are shown in Scheme 2 and Table 2, supported this view. Refluxing 1a with MgBr$_2$ in THF followed by evaporation and immediate flash chromatography (run 1, Table 2) yielded a not separable mixture ($^1$H-NMR analysis) of 50% 9a (emerging from the primary product 11a), 7% 4a, and 31% of a third product. The IR spectrum (1632 cm$^{-1}$, strong band) and in particular the $^1$H-NMR spectrum of this mixture were compatible with 6a as the third product: ($\delta$ in ppm) Me 1.46 (s); Me 1.58 (s);...
C=CH 6.93 (d, J = 9.6 Hz); comparison with 6d\textsuperscript{14,17}: Me 1.72 (s); Me 1.77 (s); C=CH 6.73 (d, J = 10.2 Hz). The structure of the supposed 6a was confirmed in a second experiment (run 2, Table 2) when the reaction mixture was worked up under conditions that favour the hydrolytic cleavage of 6a: 37% 9a and 50% tosylamide (TsNH\textsubscript{2}) were obtained from the organic layer, while isobutyaldehyde was detected in the aqueous layer by the formation of its 2,4-dinitrophenylhydrazone. Excess of MgBr\textsubscript{2} (run 3 of Table 2) did not change the ratio 6a/9a (deduced from TsNH\textsubscript{2}/9a in run 2) even with extended reaction (run 4). So, in this reaction of 1a with MgBr\textsubscript{2} the isomerization of 1a to 6a does not go to completion, perhaps because of the metathetic reaction 6a + 11a → 7a + 9a supposing that 6a is formed from the intermediate 11a through the general reaction sequence 10 → 5 → 6 (vide infra).

![Scheme 2](image)

**Scheme 2**

### Table 2. Reactions of 1a with MgBr\textsubscript{2} in Boiling THF.

<table>
<thead>
<tr>
<th>Run</th>
<th>1a [mmol]</th>
<th>MgBr\textsubscript{2} [mmol]</th>
<th>THF [ml]</th>
<th>React. Time [days]</th>
<th>Hydrolytic Work-Up</th>
<th>Yields\textsuperscript{a} [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>5</td>
<td>80</td>
<td>2.5</td>
<td>no\textsuperscript{b}</td>
<td>(7%) 4a, (31%) 6a, (50%) 9a</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>10</td>
<td>80</td>
<td>2.5</td>
<td>sustained homogeneous\textsuperscript{c}</td>
<td>50% TsNH\textsubscript{2}, 37% 9a, Me\textsubscript{2}CHCHO\textsuperscript{d}</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>20</td>
<td>80</td>
<td>2.5</td>
<td>short heterogeneous\textsuperscript{e}</td>
<td>(56%) 6a, (41%) 9a</td>
</tr>
<tr>
<td>4</td>
<td>2.5</td>
<td>30</td>
<td>40</td>
<td>7</td>
<td>short heterogeneous\textsuperscript{e}</td>
<td>(57%) 6a, (38%) 9a</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Yields in parentheses from \textsuperscript{1}H-NMR spectroscopic data.

\textsuperscript{b} Evaporation, followed by flash chromatography (silica gel, CH\textsubscript{2}Cl\textsubscript{2}).

\textsuperscript{c} Work-up as in Table 1: after adding ice, the mixture was concentrated in vacuo (bath temp. ~70 °C) and then partitioned (CH\textsubscript{2}Cl\textsubscript{2}/water).

\textsuperscript{d} Identified by the formation of its 2,4-dinitrophenylhydrazone.

\textsuperscript{e} Short partitioning between CH\textsubscript{2}Cl\textsubscript{2} and water.
The most important aspects of these experiments are the "abnormal" opening of 1 by halide and the formation of the enamide structure 6/7. As for the latter, a carbenium ion is an unlikely precursor in a Grignard solution, since rapid deprotonation should convert it to 4 that would be the final product at least for A = sulfonyl (see above). So, the enamide structure arises probably from 10. A direct conversion of 10 into 6 would be mechanistically obscure and would not lead to 3 in the reaction of 1 with RMgHal, since at least for A = sulfonyl the nitrogen of 6 would rapidly be deprotonated (forming 7), thus preventing a tautomerization of 6 into 5. The latter argument holds also for a direct conversion of 10 into 7. This reasoning was confirmed by a 72% yield of 6a when 1a reacted with a mixture of 1 equivalent of PhMgBr and 4 equivalents of MgBr₂ (vide infra). Therefore it appears reasonable to propose the reaction sequence 10 → 5 → 6, the first step having its analogue in the chemistry of epoxides. A Grignard reagent would then add to 5 forming, after protonation, the rearranged substitution product 3. This proposal requires that the latter addition is faster than the tautomerization 5 → 6. A formation of 3 by addition of RMgHal to the C=C double bond of 6 or 7 could be ruled out by quenching the reaction with D₂O (run 3 of Table 1): the ¹H-NMR spectrum of the product mixture did not reveal an incorporation of deuterium into the isopropyl group of 3aP. Since we did not observe 5a in the reactions of Table 2 we suppose that the tautomerization is accelerated by MgBr₂. So, the products 3, 4, and 6 come probably from 10, implying that in the reaction of 1 with RMgHal a certain pool of 10 is built up and maintained until the reaction goes to completion. In run 2 of Table 1, which was performed as a rough kinetic experiment, the amount of 4a (probably at least in part indicative of 10) remained constant after the initial increase while the increase in 2aP and 3aP as well as the decrease in 1a continued after the first 1.5 hours.

The abnormal opening of 1 to form 10 can be explained (1) by electrophilic assistance through one of the magnesium compounds present and (2) by the high nucleophilicity of the halide ion of the latter. The Lewis acid–Lewis base interaction (13 in Scheme 3) forces the ring opening into the borderline region. An S_N⁺⁻ like formation of a carbenium ion is unlikely both for A = sulfonyl (see above) and for A = acyl that should lead to the corresponding oxazoline: compare ref. and the literature cited therein. The double activation in 13 is expected to change the reactivity order of 1 so that 11c should form faster than 11a. A fast formation of 11c is possibly involved in run 14 of Table 1, although the extraordinary result of run 14 may be caused by a cooperation of various effects including the above discussed slowing down of the competing formation of 2cP. Irreversibility of the formation of 11c may be another one of these effects. While the anions of N-(2-halogenoalkyl) sulfonamides form rapidly the corresponding aziridines by intramolecular displacement of the halide, for the analogous
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carboxamides this cyclization is confined to some special cases\(^\text{19}\). The reaction
\(\text{1} \rightarrow \text{10}\) can therefore be expected to be reversible for \(A = \text{sulfonyl}\), but less pro-
ably for \(A = \text{acyl}\). Absence of the reverse reaction may enhance the over-all rate
\(\text{1} \rightarrow \text{5}\) and thus contribute to the result of run 14. Further aspects are considered
in the discussion of Scheme 3.

A normal opening of 1 by halide has to be taken into consideration for
strongly activated 1, but the reversibility would preclude an essential influence
of this opening on the final products.

Final proof for the deduced reaction pathway comes from two reactions of 8.
Reaction of 5 mmol 9a with 30 mmol PhMgBr yielded (after loss of some material du-
ring work-up due to emulsification) a mixture of 15% 2aP, 34% 3aP, and 11% 4a
\((^1\text{H-NMR analysis})\). The formation of 2aP requires the intermediacy of 1a, thus pro-
voking the reversibility of the abnormal opening by bromide. The second experiment
performed in the same manner with 9c provided \((^1\text{H-NMR analysis})\) 43% 3cP and 43% 6c,
but no 2cP. The structure of 6c was deduced from the \(^1\text{H-NMR}\) spectrum and confirmed
by NMR comparison with authentic material\(^\text{17}\): \((6 \text{ in ppm})\) Me 1.63 (s); Me 1.71 (s);
C=CH 6.53 (d, \(J = 10.1\) Hz). A further experiment corroborated the magnesium halide
catalysis of the tautomerization 5 \(\rightarrow\) 6 as well as the deprotonation of 6 in a
Grignard solution. Reaction of 5 mmol 1a with 5 mmol PhMgBr and 20 mmol MgBr\(_2\) pro-
vided \((^1\text{H-NMR analysis})\) 5% 2aP, 13% 3aP, 10% 4a, and 72% 6a. The ratio 2aP/3aP is
shifted from about 64:36 in runs 3-5 of Table 1 or 50:50 in run 2 to 28:72 under
the influence of the added magnesium halide. The change in the ratio
normal/abnormal opening (shown in the last column of Table 1) is even more im-
pressive: from 60:40 in runs 3-5 and 43:57 in run 2 to 5:95 in the last
experiment.

1 \[\begin{array}{c}
+ \text{MgLHal} \\
\text{- MgLHal}
\end{array}\] 13 \[\begin{array}{c}
\text{10-anti} \\
\text{base} \\
\text{H}_2\text{O}
\end{array}\] 4

10-gauche

Me

Me

\[\begin{array}{c}
\text{Me} \\
\text{Me} \\
\text{H}
\end{array}\]

5 \[\begin{array}{c}
\text{RMgHal} \\
\text{- MgLHal} \\
\text{H}_2\text{O}
\end{array}\] 3

A, L: as defined

\text{SCHEME 3}
The various pieces of evidence along with the presented arguments allow to establish a reaction scheme for the products 3 and 4: Scheme 3. The first step, i.e. the (reversible) formation of 13, may be sterically hindered as perhaps happens with 1b due to the chlorine atom at the ortho position of Dcs. Formation of 13 is followed by a borderline aziridine opening, yielding 10. This ring opening is reversible for A = sulfonyl, but the equilibrium seems to depend on the nature of the halide among other factors, I favouring 10 more than Br: comp. the last column in Table 1, runs 3-9. In analogy to the epoxide reactions 7-10 we suppose the next event to be the one-step formation of 5 by a halide displacement through a neighbouring hydride and by simultaneous elimination of MgLHal. In order to meet the stereoelectronic requirements for this process, 10 has to adopt a gauche conformation. Finally, 5 adds RmGHal in a fast reaction forming the magnesium salt of 3.

The transformation 10 → 5 may be faster for A = Piv than for A = Ts (a) due to the difference in basicity and energy of the anionic part of 10, (b) due to a lower energy of the product 5c owing to conjugation, and (c) perhaps due to a different coordination of the magnesium implicating a different stereoelectronic situation. For A = Piv coordination to the oxygen of A may be favoured while usually an electrophilic assistance of aziridine ring opening will probably operate by binding to the nitrogen (comp. the discussion in ref. 12). We consider the addition of RmGHal to 5 to be the fastest step in the sequence 1 → 10 → 5 → 4.

4 is formed from 10 exclusively (runs 6-9 of Table 1) or partly during the reaction and partly during work-up. The latter may even dominate (run 2 of Table 1). The rate ratio for the competing conversions of 10 into 4 or 5 seems to depend on Hal (comp. runs 7-9 with runs 4-6) and on R (comp. runs 4-6 with run 10 and runs 7-9 with run 11). The first influence can be explained by a steric effect on the conformational equilibrium of 10. The second influence seems also to be a steric effect, that would be comprehensible if, refining the rough picture of Scheme 3, the conversion 10 → 5 is a cyclic process (comp. ref. 7-10) producing MgLHal without intercurrent ions.

The competition between the two transformations of the imine 5 (into 6/7 or into 3) is very sensitive to the composition of the reagent as was shown above (1) by the reaction of 1a with the mixture of PhMgBr and MgBr₂ and (2) by the reaction of 9c with PhMgBr. We assume that also in the reaction of 9a with PhMgBr formation of 6a accounts for a part of the observed material loss, since 6a can only be detected if special care is taken to avoid its hydrolytic cleavage. Hydrolysis of 6a produces TsNH₂ that, dissolved in the strongly alkaline aqueous phase, would offer an explanation for the otherwise not observed extensive and sustained emulsification. The marked influence of the reagent composition is easy to understand on the basis of the proposed MgHal₂ catalysis of the tautomerization 5 → 6.
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**EXPERIMENTAL**

IR spectra (KBr tablets or film) were recorded on a Perkin-Elmer 283 spectrometer. H-NMR spectra (CDCl₃, internal TMS) were recorded on a Varian T 60-A spectrometer, operating at 60 MHz, on a Bruker HA 90-E spectrometer, operating at 90 MHz, or on a Bruker WH 250 spectrometer, operating at 250 MHz. Chemical shifts are recorded in ppm, coupling constants in Hz. The letters br, vbr, sh, s, d, t, q, m and mc denote broad, very broad, shoulder, singlet, doublet, triplet, quadruplet, multiplet, and multiplet centered at, respectively. Mass spectra were obtained from a Varian MAT 311-A spectrometer. Microanalyses were obtained from a Heraeus CHN-Rapid instrument.

**Starting Materials.**

THF was anhydrous. Magnesium bromide: magnesium bromide etherate (99%) was purchased from Aldrich and used in the supplied form. Aziridines 1a–c were prepared from 2,2-dimethylaziridine and the respective acid chloride according to a known procedure. For 1c see ref. 20.

1-(2,5-Dichlorophenyl)-2,2-dimethylaziridine (1b). Yield 92%; m.p. 80°C; IR (KBr) ν 1325, 1160/cm; H-NMR (90 MHz) δ 1.60 (s, 6H, Me, Me), 2.66 (s, 2H, CH₂), 7.27–7.80 (m, 3H, ArH); MS m/e (150°C, 37–Cl peaks omitted) 279 (M, 0.7), 238 (DCSNHCCH₂), 4, 209 (DCs, 7), 161 (3), 145 (dichlorophenyl), 9, 109 (8), 70 (M – DCs, 100). Anal. Calcd for C₁₇H₁₆Cl₂NO₂: S: C, 42.87; H, 3.96; N, 5.00. Found: C, 42.80; H, 4.04; N 4.63.

N-Methylallyl-4-toluenesulfonamide (4a). A solution of 0.1 mol sodium methoxide, and 0.1 mol methallyl chloride in 300 ml methanol was refluxed for 4 h. The mixture was evaporated to dryness, dissolved in CHCl₃, and washed with water. Subsequent chromatography (CHCl₃) provided 29% 4a. IR (film) ν 3295, 1660, 1322, 1158/cm; H-NMR (90 MHz) 6 T: 6.7 (s, 3H, Me), 2.40 (s, 3H, Me of Ts), 3.45 (d, 6.6 Hz, 2H, N–CH₂), 4.78 (br s, 1H, C=CH), 4.85 (br s, 1H, C=CH), 5.35 (br t, 6.8 Hz, 1H, NH), 7.26–7.35 (m, 2H, m–H of Ts), 7.72–7.81 (m, 2H, o–H of Ts); MS m/e (60°C) 225 (M, 13), 210 (M – Me, 2), 184 (TsnHCCH₂), 2, 155 (Ts, 24), 91 (Ts, 100). Anal. Calcd for C₁₈H₁₂NO₂S: C, 78.56; H, 6.71; N, 6.22. Found: C, 58.52; H, 6.73; N 5.93.

N-(2-Bromo-2-methylpropyl)-4-toluenesulfonamide (9a). A solution of 10 mmol 1a in 20 ml CHCl₃ was stirred with 3.4 g hydrobromic acid (48%) for 10 min. Evaporation of the organic layer provided 96% 9a. m.p. 84°C; IR (KBr) ν 3275, 1325, 1160/cm; H-NMR (90 MHz) δ 1.74 (s, 6H, Me, Re), 2.43 (s, 3H, Me of Ts), 3.15 (d, 6.8 Hz, 2H, CH₂), 5.15 (br t, 6.8 Hz, 1H, NH), 7.27–7.36 (m, 2H, m–H of Ts), 7.71–7.80 (m, 2H, o–H of Ts); MS m/e (25°C, 81–Br peaks omitted) 305 (M, 3), 226 (M – Br, 7), 184 (TsnHCCH₂), 2, 155 (T, 91), 91 (100). Anal. Calcd for C₁₈H₁₂BrNO₂S: C, 43.15; H, 5.27; N 4.57. Found: C, 43.05; H, 5.18; N, 4.76.

N-(2-Bromo-2-methylpropyl)-trimethylacetamide (9c). Preparation was analogous to 9a. Yield 94%; m.p. 39°C; IR (KBr) ν 3390, 1648, 1532/cm; H-NMR (90 MHz) δ 1.25 (s, 9H, tBu), 1.73 (s, 6H, Me, Me), 3.52 (d, 6.1 Hz, 2H, CH₂), 6.20 (vbr s, 1H, NH); MS m/e (25°C, 81–Br peaks omitted) 235.0565 (235.0558 required) 235 (M, 0.8), 220 (M – Me, 0.4), 192 (0.9), 156 (M – Br, 35), 114 (PivNHCCH₂), 37, 85 (Piv, 43), 57 (tBu, 100). Anal. Calcd for C₁₈H₂₈BrNO: C, 45.77; H, 7.68; N, 5.93. Found: C, 45.96; H, 7.58; N, 5.90.

Reactions of 1 with Grignard Reagents (Table 1).

**General Procedure.** If not otherwise stated in Table 1, the Grignard solution was prepared from 30 mmol magnesium turnings in 20 ml boiling THF by dropwise addition of 25 mmol RMgCl, dissolved in 20 ml THF, and by maintaining this mixture under reflux for 15 min. A solution of 5 mmol 1 in 40 ml THF was added under reflux and the mixture stirred under reflux for a further time given in Table 1. After cooling to room temp. cold water (D₂O in run 3) was added. The mixture was concentrated in a rotary evaporator. The aqueous residue was shaken with CH₂Cl₂, the obtained organic layer was washed with water and evaporated to dryness. The residue was analyzed by H-NMR or separated by chromatography on silica gel with CH₂Cl₂ or mixtures of CH₂Cl₂ and ethyl acetate, the percentage of the latter increasing from 0% to 100% in some cases. In run 13, 97% 2BP was eluted with 4:1 of the latter solvent mixture; elution with 3:2 yielded a mixture of (H-NMR) 0.8% 3BP, 0.4% 4BP, and 0.4% 2BP.

N-(1,1-Dimethyl-1-phenyl)-4-toluenesulfonamide (2aP). Obtained from an insufficient chromatographic separation of run 1. By recrystallizing the final eluate from ethanol. M.p. 121°C; IR (KBr) ν 3280, 1320, 1155/cm; H-NMR (90 MHz) δ 1.14 (s, 6H, Me, Me), 2.36 (s, 3H, Me of Ts), 2.84 (s, 2H, CH₂), 5.31 (br s, 1H, NH), 7.15–7.23 (m, 2H, m–H of Ts), 7.23 (s, 5H, Ph), 7.69–7.78 4(m, 2H, o–H of Ts); MS m/e (130°C) 288 (M – Me, 0.7), 260 (M – IPr, 0.6), 212 (M – benzyl, 80), 155 (Ts, 42), 91 (100). Anal. Calcd for C₁₇H₂₁NO₂S: C, 67.29; H, 6.98; N, 4.62. Found: C, 67.32; H, 7.12; N, 4.64.
N-(1-Phenyl-2-methylpropyl)-4-toluene sulfonamide (3AP). Obtained from one eluate of an insufficient chromatographic separation of run 9 by recrystallization from ethanol. M.p. 142°C; IR (KBr) ν 3290, 1325, 1165/cm; H-NMR (250 MHz) 6 0.73 (d, 6.7 Hz, 3H, Me), 0.94 (d, 6.7 Hz, 3H, Me), 1.85-1.99 (m, 1H, CH of 1Pr), 2.32 (s, 3H, Me of Ts), 4.02 (mc, 1H, N-CH), 5.29 (br d, 8.4 Hz, 1H, NH), 6.91-7.11 (m, 7H, Ph, m-H of Ts), 7.47-7.51 (m, 2H, o-H of Ts); MS m/e (100°C) 303 (M - 1), 260 (M - benzy1, 62), 155 (Ts, 37), 91 (100). Anal. Calcd for C17H23NO2S: C, 68.10; H, 7.30; N, 4.41. Found: C, 67.91; H, 7.24; N, 4.01.

N-(1-Benzyl-2-methylpropyl)-4-toluene sulfonamide (3AB). M.p. 97°C; IR (KBr) ν 3295, 1325, 1165/cm; H-NMR (250 MHz) 6 0.78 (d, 6.8 Hz, 3H, Me), 0.88 (d, 6.8 Hz, 3H, Me), 1.78-1.85 (m, 1H, CH of 1Pr), 2.40 (s, 3H, Me of Ts), 2.44-2.77 (m, 2H, CH2), 3.23-3.38 (m, 1H, N-CH), 4.31 (br d, 8.4 Hz, 1H, NH), 6.95-7.32 (m, 7H, Ph, m-H of Ts), 7.57-7.60 (m, 2H, o-H of Ts); MS m/e (120°C) 274 (M - 1Pr, 11), 226 (M - benzy1, 62), 155 (Ts, 37), 91 (100). Anal. Calcd for C18H23NO2S: C, 68.10; H, 7.30; N, 4.41. Found: C, 67.91; H, 7.24; N, 4.01.

N-(1-Dimethylpropyl)-3-aminoanisol (3AM). Oil; IR (film) ν 2980, 1342, 1168/cm; H-NMR (250 MHz) 6 0.81 (d, 6.8 Hz, 3H, Me), 0.93 (d, 6.8 Hz, 3H, Me), 1.58-1.74 (m, 1H, CH of 1Pr), 2.43 (s, 3H, Me of Ts), 3.12-3.24 (m, 1H, N-CH), 4.36 (br d, 9.3 Hz, 1H, NH), 7.28-7.31 (m, 2H, m-H of Ts), 7.75-7.78 (m, 2H, o-H of Ts); MS m/e (50°C) 241 (M, 0.9), 198 (M - 1Pr, 37), 171 (TsNH, 5), 155 (Ts, 48), 91 (100). Anal. Calcd for C12H11NO2S: C, 59.72; H, 7.93; N, 5.80. Found: C, 60.16; H, 7.62; N, 5.67.

N-(1-Dimethylpropyl)-2,5-dichlorobenzensulfonamide (2BP). M.p. 157°C; IR (KBr) ν 3250, 1655, 1450/cm; H-NMR (90 MHz) 6 1.16 (s, 6H, Me), 2.86 (s, 2H, CH2), 5.15 (br s, 1H, NH), 6.96-7.83 (m, 7H, Ph, m-H and p-H of DCs), 8.19 (mc, 1H, o-H of DCs); MS m/e (120°C, 37-CI peaks omitted) 266 (M - benzy1, 100), 209 (DCs, 30), 145 (C6H5Cl, 35), 91 (10). Anal. Calcd for C18H11Cl2NO2S: C, 53.64; H, 4.78; N, 3.59. Found: C, 53.65; H, 4.67; N, 3.65.

N-(1-Dimethylpropyl)-2,5-dichlorobenzensulfonamide (3BP). Obtained only in a mixture with 2BP and 4B. H-NMR (90 MHz) 6 0.72 (d, 6.6 Hz, 3H, Me), 0.89 (d, 6.6 Hz, 3H, Me), 1.88-2.05 (m, 1H, CH of 1Pr), 3.50 (d, 6.6 Hz, 2H, CH2), 4.86 (vbr s, 2H, C=CH2), two m for ArH seen H-NMR of 3BP (preceding compd.); peak typical of 4B in a MS of the mixture with 2BP and 4B m/e (120°C) 314 (M - 1Pr).

N-Methylallyl-2,5-dichlorobenzensulfonamide (4B). Obtained only in a mixture with 2BP and 3BP. H-NMR (90 MHz) 6 1.67 (s, 3H, Me), 3.50 (d, 6.8 Hz, 2H, CH2), 4.86 (vbr s, 2H, C=CH2), two m for ArH see H-NMR of 3BP (preceding compd.); peak typical of 4B in a MS of the mixture with 2BP and 3BP m/e (120°C) 279 (M).

N-(1-Phenylpropyl)-trimethylaceta mine (3CP). M.p. 102°C; IR (KBr) ν 3320, 1648, 1532/cm; H-NMR (250 NH) 6 0.83 (d, 6.8 Hz, 3H, Me), 0.94 (d, 6.8 Hz, 3H, Me), 1.20 (s, 3H, tBu), 1.95-2.20 (m, 1H, CH of 1Pr), 4.75 (mc, 1H, N-CH), 6.00 (br s, 1H, NH), 7.25 (s, 5H, Ph); MS m/e (40°C) 233 (M, 15), 190 (M - 1Pr, 100), 132 (M - PhN=), 7), 106 (32), 91 (23), 85 (Piv, 27), 57 (tBu, 100). Anal. Calcd for C19H23NO: C, 77.21; H, 9.94; N, 6.00. Found: C, 76.87; H, 10.13; N, 5.64.

Experiments Concerning the Reaction Mechanism

Run 2 of Table 1. Rough kinetic results. Aliquot parts were worked up according to the General Procedure of the Grignard reactions and analyzed by H-NMR.

<table>
<thead>
<tr>
<th>Time (hr)</th>
<th>[H]-[A]</th>
<th>[A]-[H]</th>
<th>[A]-[H]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 h</td>
<td>84%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>1.5 h</td>
<td>73%</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>2.5 h</td>
<td>68%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>3.5 h</td>
<td>65%</td>
<td>11%</td>
<td>11%</td>
</tr>
<tr>
<td>4.5 h</td>
<td>63%</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>5.5 h</td>
<td>60%</td>
<td>15%</td>
<td>15%</td>
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</table>

Hydrolysis of 9a,c yielding 4a or 4c and 12c, respectively. A solution of 3 mmol 9a in 10 ml THF was thoroughly mixed with 20 ml 10% aqueous sodium hydroxide solution. Shaking with CH2Cl2, separation of the two layers, and evaporation of the dried organic layer provided 9b 4a. 9c provided in the same manner a mixture of (H-NMR) ν 298 of 298°C 1165 25% of 3A and 37% of 12c. The structure of the latter product was deduced from a singlet at 7.23 ppm and a doublet (6.0 Hz) at 3.22 ppm. This assignment was supported by comparison of the pair 9d/12d by 9d singlet at 1.77 ppm and doublet (6.0 Hz) at 3.70 ppm; 12d singlet at 1.28 ppm and doublet (6.0 Hz) at 3.47 ppm.

N-Methallyl-trimethylacetamide (4c). Authentic material (for spectral comparison) was prepared by heating 1c 27 h to 100°C and recrystallizing from CH2Cl2/hexane.
Reactions of 1a with MgBr₂ (Table 2) yielding 4a, 6a, 9a, tosylamide, and isobutyraldehyde, respectively.

Run 1. The evaporated reaction mixture was taken up in CH₂Cl₂ and immediately subjected to flash chromatography (silica gel, 5 cm x 5 cm, CH₂Cl₂/MeOH). The eluate was analyzed by H-NMR.

Run 2. Work-up according to the General Procedure of the reactions with Grignard reagents. The aqueous layer and the first washing of the organic layer were caused to react with 2,4-dinitrophenylhydrazine/sulfuric acid yielding the 2,4-di-nitrophenylhydrazone of isobutyraldehyde, m.p. 181°C (lit. 182°C), mixed m.p. 181°C, IR and H-NMR spectrum identical with the spectra of authentic material. The product mixture obtained from the organic layer was chromatographed (CH₂Cl₂/ethyl acetate 4:1) yielding successively 37% 9a and 50% tosylamide.

Run 3 and run 4. The reaction mixture was evaporated to dryness. The residue was taken up in CH₂Cl₂, shortly washed twice with a small amount of water, dried, and evaporated. The residue was analyzed by H-NMR.

N-(2,2-Dimethylvinyl)-4-toluenesulfonamide (6a). Obtained in mixtures only. IR (KBr) ν 3295, 1632, 1338/cm; H-NMR (90 MHz) δ 1.46 (br s, 3H, Me), 1.60 (br s, 3H, Me), 2.40 (br d, 9.6 Hz, 1H, C=CH), 4.49 (br d, 9.6 Hz, 1H, NH), 7.25-7.33 (m, 2H, o-H of Ts), 7.51-7.59 (m, 2H, o-H of Ts); MS m/e (100°C, rel. intensity in a mixture with 2aP and 3aP) 225 (M⁺, 24), 155 (Ts, 35), 91 (100), 70 (C₆H₄N⁺, 96). Attempts to isolate and purify 6a (and 6c, vide infra), by chromatography or recrystallization were unsuccessful, partly due to the instability of the product.

Reactions of 9a,c with PhMgBr yielding 2aP, 3aP, and 4a, or 3cP and 6c, respectively.

Reaction of 9a. Reaction and work-up was analogous to the General Procedure of the reactions with Grignard reagents. The aqueous residue, obtained by addition of cold water to the reaction mixture and subsequent concentrating in vacuo, gave a stable emulsion on shaking with CH₂Cl₂. This emulsion could partially slowly (about 5 h) be broken by addition of NaCl and MgSO₄. The arising organic layer was dried, evaporated, and analyzed by H-NMR. The reaction of 9c was performed analogously without the formation of an emulsion.

N-(2,2-Dimethylvinyl)-trimethylacetamide (6c). Obtained only in a mixture with 3cP. H-NMR (90 MHz) δ 1.24 (s, 9H, tBu), 1.63 (br s, 3H, C=CH-Me), 1.71 (br s, 3H, C₃C=Me), 6.53 (br d, 10.1 Hz, further splitting recognizable, 1H, C=CH), 6.97 (br s, 1H, NH). Authentic material revealed (250 MHz) the multiplet character of the two C=CH-Me singlets and of the two doublet lines of C=CH: Coupling C=CH/Me 0.5 Hz, coupling C=CH/Me 1.4 Hz for both methyls; IR (KBr) ν 3360, 1658 sh, 1644, 1510/cm.

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13 An S_N^2-like abnormal opening may occur to some extent with a small nucleophile. Due to the distorted nature of the tert alkyl structure in \( \text{I} \), the steric demands are less stringent than in open chain tert alkyl substrates. See ref. 12.
15 The formation of a similar carbanion \( \text{O}^\cdot\text{C}^\cdot\text{N}^\cdot\text{C}^\cdot\) without stabilization by a conjugating C=C double bond has recently been described: W. Wykyspiel, J.-J. Lohmann and D. Seebach, Helv. Chim. Acta 64, 1337 (1981).
17 P. Assithianakis, J. Werry and H. Stamm, unpublished results.
23 We thank Jürgen Werry for providing us with the analytical data. J. W. was the first one to isolate 4c in a pure state.